VERIFICATION OF TRANSLATION

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INHALATION DEVICE FOR TRANSPULMONARY ADMINISTRATION

[Claims]

[Claim 1] An inhalation device for transpulmonary administration comprising:

a chamber for containing a pharmaceutical composition which is pulverized into fine particles by an air-generated impact for dispersal in air;

an air inlet flow path for introducing to the chamber outside air to apply the air-generated impact to the pharmaceutical composition and for injecting the outside air toward the pharmaceutical composition;

an inhalation flow path having a suction port facing the chamber to inhale the pulverized pharmaceutical composition;

a housing for accommodating the chamber, the air inlet flow path, and the inhalation flow path;

a mouthpiece provided at one end of the housing, the mouthpiece being provided with a mouth-side flow path which communicates with the inhalation flow path and an auxiliary flow path for directly inhaling the outside air which does not communicate with the inhalation flow path and the mouth-side flow path;

wherein the air-generated impact is applied to the

pharmaceutical composition by the outside air which flows into the chamber by inhalation-induced pressure generated when a user (patient) inhales air, and the pulverized pharmaceutical composition is introduced to the mouth-side flow path, and at the same time the outside air is directly introduced to the auxiliary flow path by the inhalation-induced pressure.

[Claim 2] An inhalation device for transpulmonary administration comprising:

a chamber for containing a pharmaceutical composition which is pulverized into fine particles by an air-generated impact for dispersal in air;

an air inlet flow path for introducing to the chamber outside air to apply the air-generated impact to the pharmaceutical composition and for injecting the outside air toward the pharmaceutical composition;

an inhalation flow path having a suction port facing the chamber to inhale the pulverized pharmaceutical composition;

a housing for accommodating the chamber, the air inlet flow path, and the inhalation flow path;

a mouthpiece provided at one end of the housing, the mouthpiece being provided with a mouth-side flow path which communicates with the inhalation flow path and a divider having an orifice in at least one of the mouth-side flow path or the

inhalation flow path for reducing the diameter of the flow path by forming a step part;

wherein the air-generated impact is applied to the pharmaceutical composition by the outside air which flows into the chamber by inhalation-induced pressure generated when a user (patient) inhales air so that the pulverized pharmaceutical composition is introduced to the inhalation flow path and the mouth-side flow path, and also passes through the orifice.

[Claim 3] The inhalation device for transpulmonary administration according to Claim 2, wherein a plurality of the dividers each having at least one orifice is provided at appropriately spaced intervals.

[Claim 4] The inhalation device for transpulmonary administration according to Claim 2 or 3,

wherein the mouthpiece is provided with an auxiliary flow path for directly inhaling the outside air which does not communicate with the inhalation flow path and the mouth-side flow path; and

wherein the pulverized pharmaceutical composition is introduced to the inhalation flow path and the mouth-side flow path, and at the same time the outside air is directly introduced to the auxiliary flow path by the

inhalation-induced pressure.

[Claim 5] The inhalation device for transpulmonary administration according to any of Claims 1 through 4, comprising:

the chamber for containing a vessel sealed by a sealing member which contains a freeze-dried pharmaceutical composition in a non-powder cake-like form which disperses in air by an air-generated impact; and

an unsealing member for releasing the sealed condition provided by the sealing member;

wherein the vessel is unsealed by the unsealing member to establish communication between the suction port and the inside of the vessel; and

the air-generated impact is applied by the inhalation-induced pressure to the pharmaceutical composition contained in the vessel.

[Claim 6] The inhalation device for transpulmonary administration according to any of Claims 1 through 5, further comprising a check valve to prevent the pulverized pharmaceutical composition from flowing to the outside through the air inlet flow path.

[Detailed Description of the Invention]

[0001]

[Technical Field to Which the Invention Pertains]

The present invention relates to a self-inhaling type inhalation device for transpulmonary administration.

[0002]

[Prior Art]

Such inhalation devices are provided with a chamber for containing a pharmaceutical composition, and are configured in such a way that outside air is introduced to the chamber by the inhalation-induced pressure of a user (patient) to apply an air-generated impact to the pharmaceutical composition, thus pulverizing the pharmaceutical composition into fine particles so that the user (patient) can inhale the pulverized pharmaceutical composition into the lungs from the mouth-side flow path (refer to Patent Document 1, for example).

[0003]

Such an inhalation device disadvantageously places a burden on users (patients) who have reduced pulmonary capacity or children (patients) when generating the air impact with his/her inhalation-induced pressure.

[0004]

This burden on the user can be reduced by providing an auxiliary flow path which directly reaches the mouth-side flow path of the mouthpiece, not via the chamber, so that he/she

can inhale outside air which is not used for applying air impact to the pharmaceutical composition (auxiliary air). This auxiliary is inhaled and thus, the air flow rate can be further increased. Therefore, the generated fine particles air can be efficiently delivered to the lungs.

[0005]

However, because fine particles easily coalesce/agglomerate, they tend to form coalesced or agglomerated masses due to disturbances in the air flow within the mouth-side flow path of the mouthpiece that are caused when the auxiliary air is mixed with air containing the pulverized pharmaceutical composition. Thus, some of the pulverized pharmaceutical composition does not reach the user's (patient's) lungs and adheres to his/her throat.

[0006]

The pulverized pharmaceutical composition is partially dispersed in the form of agglomerated masses of fine particles when the air-generated impact applied to the pharmaceutical composition is insufficient.

[0007]

[Patent Document 1]

Japanese Published Unexamined Patent Application No. 1999-221280 (all pages, all figures)

[0008]

[Problem to Be Solved by the Invention]

In view of the above-described problems, the present invention provides an inhalation device for transpulmonary administration which can prevent agglomerated masses of fine particles of the pharmaceutical composition from entering the user's (patient's) mouth.

[0009]

[Means for Solving the Problem]

According to the present invention of the first aspect, an inhalation device for transpulmonary administration comprising: a chamber for containing a pharmaceutical composition which is pulverized into fine particles by an air-generated impact for dispersal in air; an air inlet flow path for introducing to the chamber outside air to apply the air-generated impact to the pharmaceutical composition and for injecting the outside air toward the pharmaceutical composition; an inhalation flow path having a suction port facing the chamber to inhale the pulverized pharmaceutical composition; a housing for accommodating the chamber, the air inlet flow path, and the inhalation flow path; a mouthpiece provided at one end of the housing, the mouthpiece being provided with a mouth-side flow path which communicates with the inhalation flow path and an auxiliary flow path for directly inhaling the outside air which does not communicate with the inhalation flow path and the mouth-side flow path; wherein the air-generated impact is applied to the

pharmaceutical composition by the outside air which flows into the chamber by inhalation-induced pressure generated when a user (patient) inhales air, and the pulverized pharmaceutical composition is introduced to the mouth-side flow path, and at the same time the outside air is directly introduced to the auxiliary flow path by the inhalation-induced pressure.

[0010]

According to the present invention of the second aspect, an inhalation device for transpulmonary administration comprising: a chamber for containing a pharmaceutical composition which is pulverized into fine particles by an air-generated impact for dispersal in air; an air inlet flow path for introducing to the chamber outside air to apply the air-generated impact to the pharmaceutical composition and for injecting the outside air toward the pharmaceutical composition; an inhalation flow path having a suction port facing the chamber to inhale the pulverized pharmaceutical composition; a housing for accommodating the chamber, the air inlet flow path, and the inhalation flow path; a mouthpiece provided at one end of the housing, the mouthpiece being provided with a mouth-side flow path which communicates with the inhalation flow path and a divider having an orifice in at least one of the mouth-side flow path or the inhalation flow path for reducing the diameter of the flow path by forming a step part; wherein the air-generated impact is applied to

the pharmaceutical composition by the outside air which flows into the chamber by inhalation-induced pressure generated when a user (patient) inhales air so that the pulverized pharmaceutical composition is introduced to the inhalation flow path and the mouth-side flow path, and also passes through the orifice.

[0011]

It is preferred that a plurality of the dividers each having at least one orifice is provided at appropriately spaced intervals.

[0012]

It is preferred that the inhalation device for transpulmonary administration comprises the chamber for containing a vessel sealed by a sealing member which contains a freeze-dried pharmaceutical composition in a non-powder cake-like form which disperses in air by an air-generated impact; and an unsealing member for releasing the sealed condition provided by the sealing member; wherein the vessel is unsealed by the unsealing member to establish communication between the suction port and the inside of the vessel; and the air-generated impact is applied by the inhalation-induced pressure to the pharmaceutical composition contained in the vessel.

[0013]

It is preferred that the inhalation device for

transpulmonary administration further comprises a check valve to prevent the pulverized pharmaceutical composition from flowing to the outside through the air inlet flow to the outside path even when the user (patient) erroneously blows air instead of inhaling air.

[0014]

[Mode for Carrying Out the Invention]

Hereinafter, an inhalation device of the present invention will be described according to its embodiments with reference to drawings attached hereto. Figs. 1 through 8 show an inhalation device according to the first embodiment and Figs. 9 through 12 show an inhalation device according to the second embodiment.

[0015]

Embodiment 1

The inhalation device comprises a needle part 3 (an example of an unsealing member) in which are formed an inhalation flow path 1 and an air inlet flow path 2, a holder part 5 for holding a vessel 4 which contains one dose of pharmaceutical composition A and is sealed by a stopper 4a (an example of a sealing member), a chamber 6 for containing the vessel 4 in the holder part 5, a guide part 7 for guiding the holder part 5 in the axial direction of the needle part 3, and a holder operating part 15 for advancing and retreating the holder part 5 along the guide part 7; these are all housed

in a tubular housing 9. Moreover, a mouthpiece 10 is provided at a tip of the housing 9.

[0016]

The pharmaceutical composition A can be pulverized into fine particles, in an instant or immediately, having a particle size suitable for transpulmonary administration by an air-generated impact that flows into the vessel. The present embodiment employs a freeze-dried composition, which will be explained in more detail later.

[0017]

As shown in Fig. 5, the housing 9 is provided with a housing main body 9B in which is formed a removal/insertion port 9A in which the holder part 5 is in a retreated position, and a lid 9C that opens and closes the removal/insertion port 9A. The lid 9C is connected to the housing main body 9B by a hinge 9D, and a window 9E for verifying whether the vessel 4 has been loaded is provided on the lid 9C.

[0018]

An inlet port 9F for introducing outside air is provided on a wall of the housing 9. The inlet port 9F is equipped with a check valve 9G for preventing the pulverized pharmaceutical composition A from flowing out.

[0019]

A flange-shaped partition part 3A is formed at the base end of the needle part 3, and an end of the air inlet

flow path 2 of the needle part 3 opens at an outer wall surface of the partition part 3A through the inside of the partition part 3A. Moreover, a peripheral wall part 3B extends from an outer end part of the partition part 3A to the front. An engagement hole 3C is formed at the peripheral wall part 3B. An engagement projection 3D is formed at a part inserted into the front from the needle part 3, and the inhalation flow path 1 opens at the tip portion through the engagement projection 3D.

[0020]

The needle part 3 is attached to the housing 9 by fitting the partition part 3A of the needle part 3 into the tip part of the housing 9. Furthermore, the axial direction of the housing 9 and the axial direction of the needle part 3 are aligned with each other.

[0021]

The mouthpiece 10 is provided with a mouth-side flow path 11 and an auxiliary flow path 12. More specifically, the mouthpiece 10 consists of the mouth-side flow path 11 which communicates with the inhalation flow path 1 of the needle part 3 so as to introduce the pulverized pharmaceutical composition A into the user's (patient's) mouth, and the auxiliary flow path 12 which does not communicate with the inhalation flow path 11 so as to introduce outside air directly into the user's (patient's) mouth.

[0022]

The mouth-side flow path 11 passes through the mouthpiece 10. The front end and rear end of the mouth-side flow path 11 open at the front side and the rear side of the mouthpiece 10, respectively, to form a front opening 11A and a rear opening 11B. An engagement concave portion 11C is formed at the rear opening 11B. As shown in Fig. 6, a divider 13 having an orifice 13A is provided in the mouth-side flow path 11. The center of the orifice 13A is positioned at the center of the axis of the mouth-side flow path 11 of the mouthpiece 10.

[0023]

The auxiliary flow path 12 is formed annularly around the mouth-side flow path 11 as shown in Fig. 4. At the rear end of the auxiliary flow path 12 is formed an auxiliary air inlet port 12C which opens at the rear surface of the mouthpiece 10 so as to introduce outside air. The tip portion of the auxiliary flow path 12 is branched to form a plurality of inhaling branched paths 12A. These branched paths 12A open at the front surface of the mouthpiece 10 to form auxiliary openings 12B. These auxiliary openings 12B surround the front opening 11A of the mouth-side flow path 11. Thus, when a user has the mouthpiece 10 in his/her mouth, the front opening 11A of the mouth-side flow path 11 and the auxiliary openings 12B of the auxiliary flow path 12 are located in the user's mouth.

[0024]

The mouthpiece 10 is provided with a pair of attachment portions 14 extending toward the rear of the mouthpiece 10 in the vertical direction, and the attachment portion 14 each is provided with an engagement projection 14A.

[0025]

The engagement projection 3D of the needle part 3 is engaged with the engagement concave portion 11C of the rear opening 11B of the mouth-side flow path 11 of the mouthpiece 10 to communicate between the inhalation flow path 1 and the mouth-side flow path 11. In addition, the pair of vertically provided attachment portions 14 are fitted into the peripheral wall part 3B of the needle part 3 to engage the engagement projections 14A of the attachment portions 14 with the engagement holes 3C formed at the peripheral wall part 3B of the needle part 3, thus fixing the mouthpiece 10 to the needle part 3.

[0026]

The above-described configuration prevents communication between a main flow path, which allows the user to inhale the pulverized pharmaceutical composition A into his/her mouth by the inhalation flow path 1 of the needle part 3 and the mouth-side flow path 11 of the mouthpiece 10, and a sub flow path, which allows the user to inhale auxiliary air introduced from the auxiliary air inlet port 12A by the

auxiliary flow path 12. Therefore, the auxiliary air can flow directly into the user's mouth.

[0027]

The holder operating part 15, which is another one of the elements constituting the inhalation device, comprises a mechanism 15A for moving the holder part 5 back and forth along the axial direction of the housing 9, and an operating lever for operating the mechanism 15A. The mechanism 15A has a connector 15B, one end of which is connected to the holder part 5 by a hinge 5A, and the other end of which is connected to the lid 9C by a hinge 91A. The lid 9C also serves as the above-mentioned operating lever. By opening and closing the lid 9C, the holder part 5 is advanced and retreated along the guide part 7. The holder part 5 is provided with a remover 16 for lifting the vessel 4 from the base thereof to remove the vessel 4, and a lever 17 for lifting the vessel 4 is formed on the remover 16.

[0028]

The inhalation device is used as follows. Firstly, the lid 9C is lifted to open the removal/insertion port 9A of the housing 9 as shown in Fig. 5, whereby the holder part 5 is pulled backward to reach the removal/insertion port 9A of the housing 9. Next, the vessel 4 is attached to the holder part 5 with the stopper 4a facing forward. Next, the lid 9C is pushed down to close the removal/insertion port 9A of the

housing 9 as shown in Fig. 6, whereby the holder part 5 is pushed toward the needle part 3 by the connector 15B, and the stopper 4a of the vessel 4 is pierced by the tip of the needle part 3, thus placing the inhalation flow path 1 and the air inlet flow path 2 of the needle part 3 in communication with the inside of the vessel 4.

[0029]

Subsequently, the user takes the mouthpiece 10 in his/her mouth and inhales air from the vessel 4 through both the mouth-side flow path 11 and the auxiliary flow path 12 of the mouthpiece 10 via the inhalation flow path 1 of the needle part 3 by the user's (patient's) inhalation-induced pressure. During this process, the inside of the vessel 4 becomes subject to negative pressure and thus the check valve 9G opens, and outside air flows into the vessel 4 through the air inlet flow path 2 of the needle part 3. As a result, an air-generated impact is created in the vessel 4, the pharmaceutical composition A is pulverized into fine particles, and the fine particles are delivered into the user's (patient's) lungs from the inhalation flow path 1 and the mouth-side flow path 11. At the same time, the auxiliary air is directly inhaled into the user's (patient's) mouth via the auxiliary flow path 12 from the auxiliary air inlet port. As described above, the auxiliary air is not mixed with air containing the pulverized pharmaceutical composition A

flowing through the inhalation flow path 1 and the mouth-side flow path 11, which prevents the coalescence/agglomeration of fine particles due to the flow of the auxiliary air. By allowing inhalation of the auxiliary air, the inhalation device can thus reduce the burdens on a user (patient) having reduced pulmonary capacity or the burden on a child (patient).

[0030]

Even if the pharmaceutical composition A were to be partially dispersed in the form of agglomerated masses because a user's (patient's) inhalation strength is weak, the agglomerated masses would be crushed against the divider 13 located at the periphery of the orifice 13A in the mouth-side flow path 11 of the mouthpiece 10 and thus dispersed and pulverized into fine particles when the agglomerated masses pass through the orifice 13A. The agglomerated masses formed when passing through the mouth-side flow path 11 are also dispersed through the divider 13.

[0031]

The check valve 9G prevents the pulverized pharmaceutical composition A from flowing to the outside from the inlet port even when the user (patient) erroneously blows air into the vessel 4 from the mouth-side flow path 11 of the mouth piece 10.

[0032]

After transpulmonary administration is completed,

the lid 9C is lifted to pull the holder part 5 back up to the removal/insertion port 9A of the housing 9 as shown in Fig. 7, and then the remover 16 is lifted by the lever 17 and the vessel 4 is removed from the holder part 5 as shown in Fig. 8.

[0033]

When the inhalation device is not being used, the mouthpiece 10 is closed with a cap 18 as shown in Fig. 1.

[0034]

As described above, the air flow rate of one inhalation by the user (patient) is generally in the range of 5 to 300 L/min. Considering the possible respiratory ability of the user (patient), the inhalation device of the present invention is set so that the volume of the vessel 4 is about 5 ml, the bore (diameter) of the air inlet flow path 2 is about 2 mm, the bore (diameter) of the inhalation flow path 1 is about 2 mm, and the bore (diameter) of the inhaling branched path 12A is about 0.7 mm.

[0035]

Embodiment 2

As shown in Figs. 9 and 10, an inhalation device of the present embodiment is provided with two dividers 13 and 131 that are formed along the mouth-side flow paths 11 and 111 of the mouthpiece 10 at appropriately spaced intervals. The components constituting the device other than the

mouthpiece 10 are the same or similar to those of the first embodiment, and thus the same or similar components are designated by the same numerals as in the first embodiment, and their detailed descriptions are omitted here.

[0036]

A single orifice 13A, the center of which is positioned at the center of the axis of the mouth-side flow path 11 of the mouthpiece 10, is formed at the divider 13 in the front part of the mouthpiece. A plurality of orifices 13A are provided at substantially equally spaced intervals at the divider 131 in the rear part of the mouthpiece, as shown in Fig. 11.

[0037]

The mouthpiece 10 is comprised of two separable parts: a front part and a rear part. The divider 13 is formed in a front divided body 101 while the divider 131 is formed in a rear divided body 102.

[0038]

As shown in Fig. 12, the front divided body 101 is provided with a mouth-side flow path 11 and an auxiliary flow path 12 as in the mouthpiece 10 of the first embodiment. An engagement concave portion 11C is formed at a rear opening 11B of the mouth-side flow path 11. An engagement concave portion 101A is formed at an inner wall of the auxiliary flow path 12. As shown in Fig. 11, the rear divided body 102 is

configured by integrating an internal tube 102A containing the mouth-side flow path 111 and an external tube 102B. The external tube 102B is provided with engagement projections 102C and 102D.

[0039]

The tip of the internal tube 102A of the rear divided body 102 is fitted to the engagement concave portion 11C of the front divided body 101 and the engagement projection 102D of the external tube 102B is engaged with the engagement concave portion 101A of the front divided body 101. This establishes connection between the front and rear divided bodies 101 and 102. The external tube 102B of the rear divided body 102 is engaged with the peripheral wall part 3B of the needle part 3, the engagement projection 102C of the external tube 102B is engaged with the engagement hole 3C of the peripheral wall part 3B, and the internal tube 102A is engaged with the engagement projection 3D of the needle part 3. The mouthpiece 10 is thus positioned at the tip of the housing 1.

[0040]

The inhalation device of the present embodiment is used in the same manner as described above. The auxiliary air is introduced from the auxiliary air inlet port 12A of the front divided body 101 of the mouthpiece 10 as shown by an arrow in Fig. 10.

[0041]

The dividers 13 and 131 are provided at two locations in the mouth-side flow path 11 of the mouthpiece 10, thus allowing them to expedite the dispersal of agglomerated masses of fine particles of the pharmaceutical composition. Dividers may also be provided at three or more locations.

[0042]

Figs. 13 through 15 show examples of other embodiments. In the inhalation device shown in Fig. 13, an operating member 19 is arranged in such a way that it can be rotated in both forward and reverse circumferential directions of the housing 9 as shown by the arrows. The mechanism of the holder operating part, which is not shown in the drawing, is provided with a spiral groove and a follower that engages therewith; when the operating member 19 is rotated forward or reverse, this rotation is converted to a linear movement (back and forth movement) of the holder part 5 in the axial direction of the needle part 3. The rotation angle of the operating member 19 is substantially 180°C. The inhalation devices shown in Figs. 14 and 15 are rotatably provided with an annular operating member 19 at the housing 9. The mechanism of the holder operating part, which is not shown in the drawing, comprises a feed screw; when the operating member 19 is rotated, this rotation is converted to linear movement of the holder part 5 in the axial direction

of the needle part 3. The holder part 5 can be withdrawn from the back of the housing 9. The other composite parts such as the mouthpiece 10, are the same as in the first embodiment.

[0043]

Freeze-dried pharmaceutical composition

A freeze-dried pharmaceutical composition is prepared in a non-powder dry form by pouring a solution containing a single effective dose of a drug into a vessel and then freeze-drying it as is. The non-powder-form freeze-dried pharmaceutical composition can be manufactured by a manufacturing method ordinarily used for freeze-dried preparations (freeze-dried pharmaceutical composition), such as an injection that is dissolved at the time of use by selecting a suitable composition (types and amounts of active ingredient and carrier used together with the active ingredient) such that the disintegration index of the freeze-dried pharmaceutical composition prepared is 0.015 or more, and the freeze-dried pharmaceutical composition can be made into fine particles down to a particle diameter suitable for transpulmonary administration by the impact of outside air introduced into the vessel.

[0044]

The disintegration index in the present invention is a value particular to the freeze-dried pharmaceutical composition that can be obtained by measuring the composition

according to the following method.

<Disintegration index>

0.2 to 0.5 ml of a mixture containing target components that will constitute the freeze-dried composition is poured into a vessel having a trunk diameter of 18 mm or 23 mm, and is subjected to freeze-drying. Next, 1.0 ml of n-hexane is instilled gently down the wall of the vessel onto the non-powder-form freeze-dried pharmaceutical composition obtained. The mixture is agitated for about 10 seconds at 3,000 rpm, and is then put into a UV cell with an optical path length of 1 mm and an optical path width of 10 mm, and the turbidity is measured immediately at a measurement wavelength of 500 nm using a spectrophotometer. The measured turbidity is divided by the total amount (weight)) of the components constituting the freeze-dried pharmaceutical composition, and the value obtained is defined as the disintegration index.

Here, an example of the lower limit of the disintegration index of a freeze-dried pharmaceutical composition of the present invention can be given as the above-mentioned 0.015, preferably 0.02, more preferably 0.03, yet more preferably 0.04, still more preferably 0.05, and most preferably 0.1. Moreover, there is no particular restriction on the upper limit of the disintegration index of the freeze-dried pharmaceutical composition of the present invention, but an example can be given as 1.5, preferably 1,

more preferably 0.9, yet more preferably 0.8, and still more preferably 0.7. The freeze-dried pharmaceutical composition of the present invention preferably has a disintegration index in a range including lower and upper limit selected as appropriate from the above, provided that the disintegration index is at least 0.015. Specific examples of the range of the disintegration index are 0.015 to 1.5, 0.02 to 1.0, 0.03 to 0.9, 0.04 to 0.8, 0.05 to 0.7 and 0.1 to 0.7.

Moreover, it is preferable to prepare the freeze-dried pharmaceutical composition of the present invention in a non-powder cake-like form through freeze-drying. In the present invention, 'non-powder-form freeze-dried pharmaceutical composition' means a dry solid obtained by freeze-drying a solution, and is generally called a 'freeze-dried cake'. However, even if cracks appear in the cake, the cake breaks into a plurality of large lumps, or part of the cake breaks into a powder during the freeze-drying process or during subsequent handling, this cake is still included as a non-powder-form freeze-dried pharmaceutical composition that is the subject of the present invention, provided the effects of the present invention are not impaired.

[0045]

As described above, the freeze-dried pharmaceutical composition of the present invention has a disintegration index of 0.015 or more and a non-powder

cake-like form and becomes fine particles having a mean particle diameter of 10 microns or less or a fine particle fraction of 10% or more from an air-generated impact having an air speed of at least 1 m/sec and an air flow rate of at least 17 ml/sec based on the specific property particular to the freeze-dried pharmaceutical composition characterized by the above-described disintegration index.

[0046]

A preferable freeze-dried pharmaceutical composition is such that, from the above air-generated impact, the mean particle diameter becomes 10 microns or less and preferably 5 microns or less or the proportion of effective particles (fine particle fraction) of 10% or more, preferably 20% or more, more preferably 25% or more, still more preferably 30% or more, and most preferably 35% or more.

[0047]

As described above, the air-generated impact applied to the freeze-dried pharmaceutical composition is not limited, as long as it is generated by air having an air speed of at least 1 m/sec and an air flow rate of at least 17 ml/sec. Specific examples of an air-generated impact include an impact generated by air having a speed of 1 m/sec or more, preferably 2 m/sec or more, more preferably 5 m/sec or more and still more preferably 10m/sec or more. Here, there is no restriction on the upper limit of the air speed, but it is

generally 300 m/sec, preferably 250 m/sec, more preferably 200 m/sec and yet more preferably 150 m/sec. The air speed is not limited and can be selected to be in a range with any of the above-described lower and upper limits; specifically, however, the ranges of 1 to 300 m/sec, 1 to 250 m/sec, 2 to 250 m/sec, 5 to 250 m/sec, 5 to 200 m/sec, 10 to 200 m/sec or 10 to 150 m/sec can be mentioned.

[0048]

Examples of air-generated impact include those generated by air having an air flow rate of generally 17 ml/sec or more, preferably 20 ml/sec or more and more preferably 25 ml/sec or more. There is no particular restriction on the upper limit of the air flow rate; however, the air flow rate is generally 900 L/min, preferably 15 L/sec, more preferably 5 L/sec, yet more preferably 4 L/sec, and most preferably 3 L/sec. More specifically, the air flow rate is not limited and can be selected to be in a range with any of the above-described lower and upper limits; specifically, however, examples of such a range include 17 ml/sec to 15 L/sec, 20 ml/sec to 10 L/sec, 20 ml/sec to 5 L/sec, 20 ml/sec to 4 L/sec, 20 ml/sec to 3 L/sec and 25 ml/sec to 3 L/sec.

[0049]

[Effects of the Invention]

The inhalation device according to Claim 1 is provided with a mouthpiece having a mouth-side flow path

communicating with an inhalation flow path, and an auxiliary flow path for directly inhaling outside air which does not communicate with the inhalation flow path and the mouth-side flow path, and is configured in such a way that outside air is directly introduced to the auxiliary flow path by the inhalation-induced pressure of a user (patient). Therefore, the auxiliary air does not collide with air containing the pulverized pharmaceutical composition, and thus the fine particles can be prevented from coalescing/agglomerating due to the flow of the auxiliary air. Auxiliary air containing no pharmaceutical composition is inhaled and thus, the air flow rate can be further increased. Therefore, the fine particles that are generated can be efficiently delivered to the lungs.

[0050]

The inhalation device according to Claim 2 is configured such that at least one of the mouth-side flow path or the inhalation flow path is provided with a divider having an orifice for reducing the diameter of the flow path by forming the step part. Thus, agglomerated masses of fine particles of the pharmaceutical composition passing through the mouth-side flow path of the mouthpiece can be dispersed.

[0051]

The inhalation device according to Claim 3 is configured such that a plurality of the dividers having an

orifice are formed at appropriately spaced intervals, and thus, agglomerated masses of the pharmaceutical composition can be further dispersed.

[0052]

The inhalation device according to Claim 4 is configured such that fine particles can be prevented from coalescing/agglomerating due to the flow of the auxiliary air which occurs in the prior art, and further, agglomerated masses of fine particles of the pharmaceutical composition passing through the mouth-side flow path of the mouthpiece can be dispersed. Therefore, agglomerated masses of fine particles of the pharmaceutical composition can be prevented from entering the user's (patient's) mouth.

[0053]

According to the inhalation device of Claim 5, air containing the pulverized freeze-dried pharmaceutical composition is not mixed with the auxiliary air, and the divider can disperse agglomerated masses of fine particles of the pharmaceutical composition.

[0054]

According to the inhalation device of Claim 6, a check valve is provided for preventing the fine particles from flowing to the outside from the air inlet flow path even when the user (patient) mistakenly blows air instead of inhaling it.

[Brief Description of the Drawings]

[Figure 1] A perspective view showing an inhalation device according to the first embodiment of the present invention.

[Figure 2] A longitudinal cross section showing the inhalation device.

[Figure 3 (a)] An enlarged longitudinal cross section showing the inhalation device.

[Figure 3 (b)] An enlarged horizontal cross section showing the inhalation device.

[Figure 4 (a)] An enlarged elevation view showing the mouthpiece.

[Figure 4 (b)] An enlarged longitudinal cross section showing the mouthpiece.

[Figure 4 (c)] An enlarged horizontal cross section showing the mouthpiece.

[Figure 4 (d)] An enlarged rear view showing the mouthpiece.

[Figure 5] A longitudinal cross section showing the operation of the inhalation device.

[Figure 6] A longitudinal cross section showing the operation of the inhalation device.

[Figure 7] A longitudinal cross section showing the operation of the inhalation device.

[Figure 8] A longitudinal cross section showing

the operation of the inhalation device.

[Figure 9] A perspective view of an inhalation device according to the second embodiment of the present invention.

[Figure 10] An enlarged elevation view of the inhalation device.

[Figure 11 (a)] An enlarged elevation view of the rear divided body that forms part of the mouthpiece of the inhalation device.

[Figure 11 (b)] An enlarged longitudinal cross section showing the mouthpiece.

[Figure 11 (c)] An enlarged horizontal cross section showing the mouthpiece.

[Figure 11 (d)] An enlarged rear view showing the mouthpiece.

[Figure 12 (a)] An enlarged elevation view showing the front divided body that forms part of the mouthpiece.

[Figure 12 (b)] An enlarged longitudinal cross section showing the mouthpiece.

[Figure 12 (c)] An enlarged horizontal cross section showing the mouthpiece.

[Figure 12 (d)] An enlarged rear view showing the mouthpiece.

[Figure 13] A perspective view showing an inhalation device according to another embodiment of the

present invention.

[Figure 14] A perspective view showing an inhalation device according to another embodiment of the present invention.

[Figure 15] A perspective view showing a dry powder inhalation device according to another embodiment when not in use.

[Explanation of Reference Numerals]

A pharmaceutical composition

1 inhalation flow path

2 air inlet flow path

3 needle part (unsealing member)

6 chamber

9 housing

9G check valve

10 mouthpiece

11 mouth-side flow path of the mouthpiece

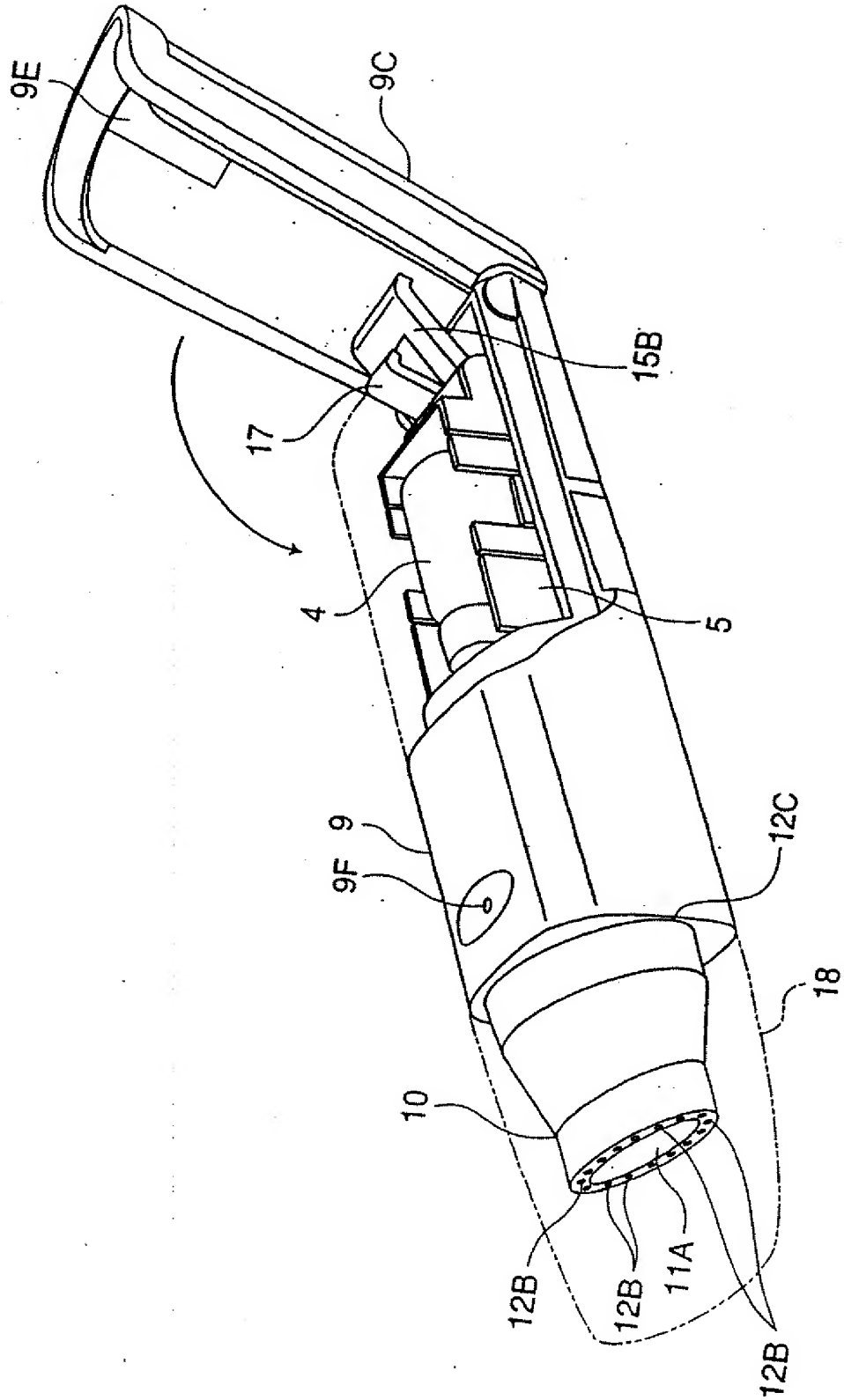
12 auxiliary flow path of the mouthpiece

13 divider

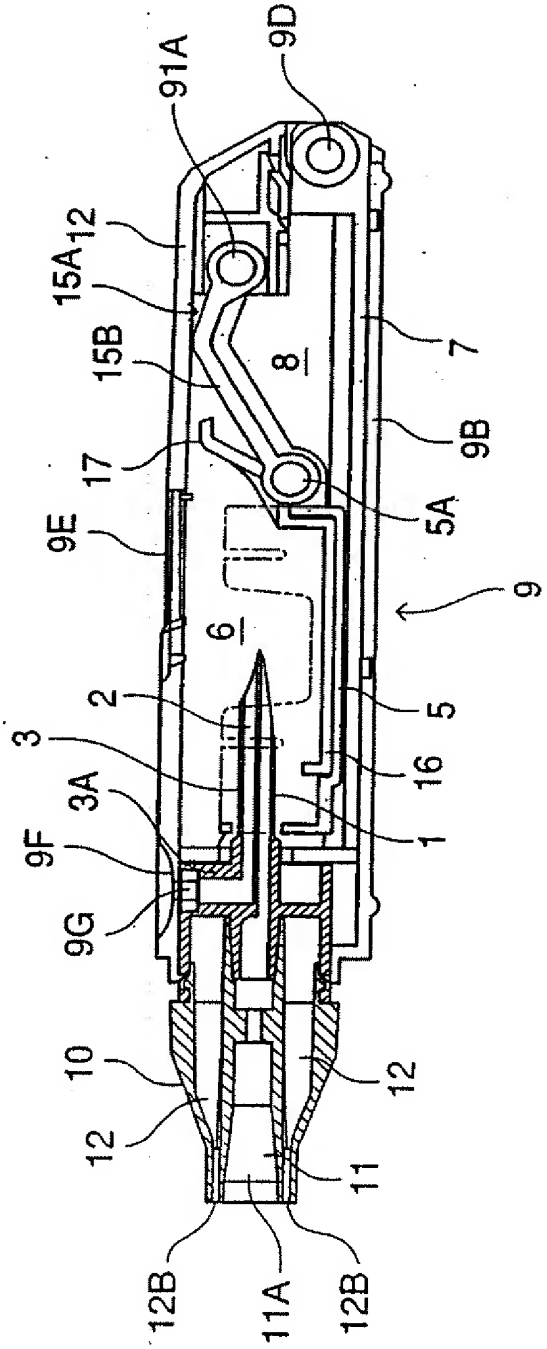
13A orifice

[Document Name] Drawings

[Figure 1]



[Figure 2]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15B
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9B
17
5A
9E
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9G
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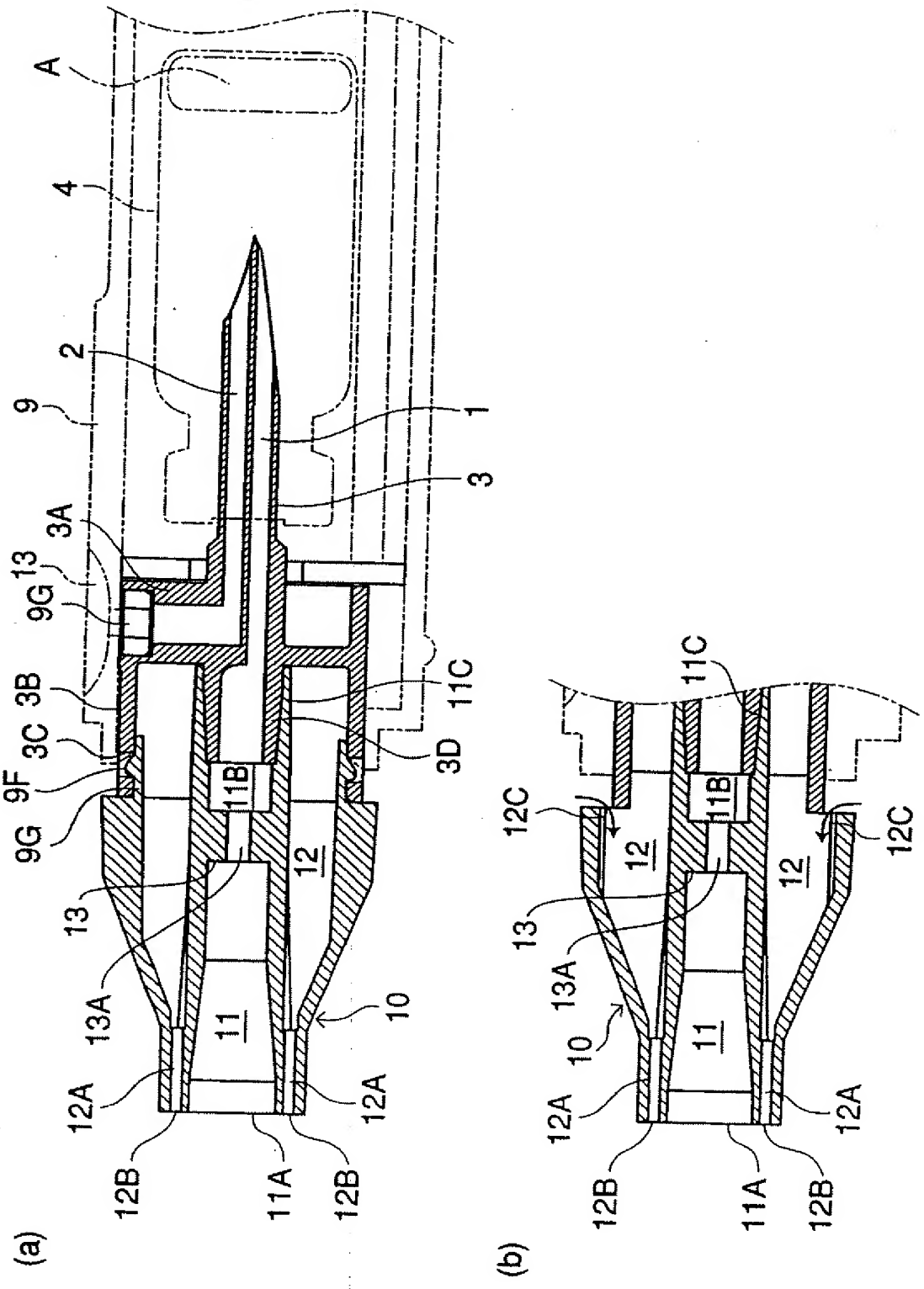
12
11
12B
11A
12B

[Figure 3]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12B
11A
12B
12A
(b)
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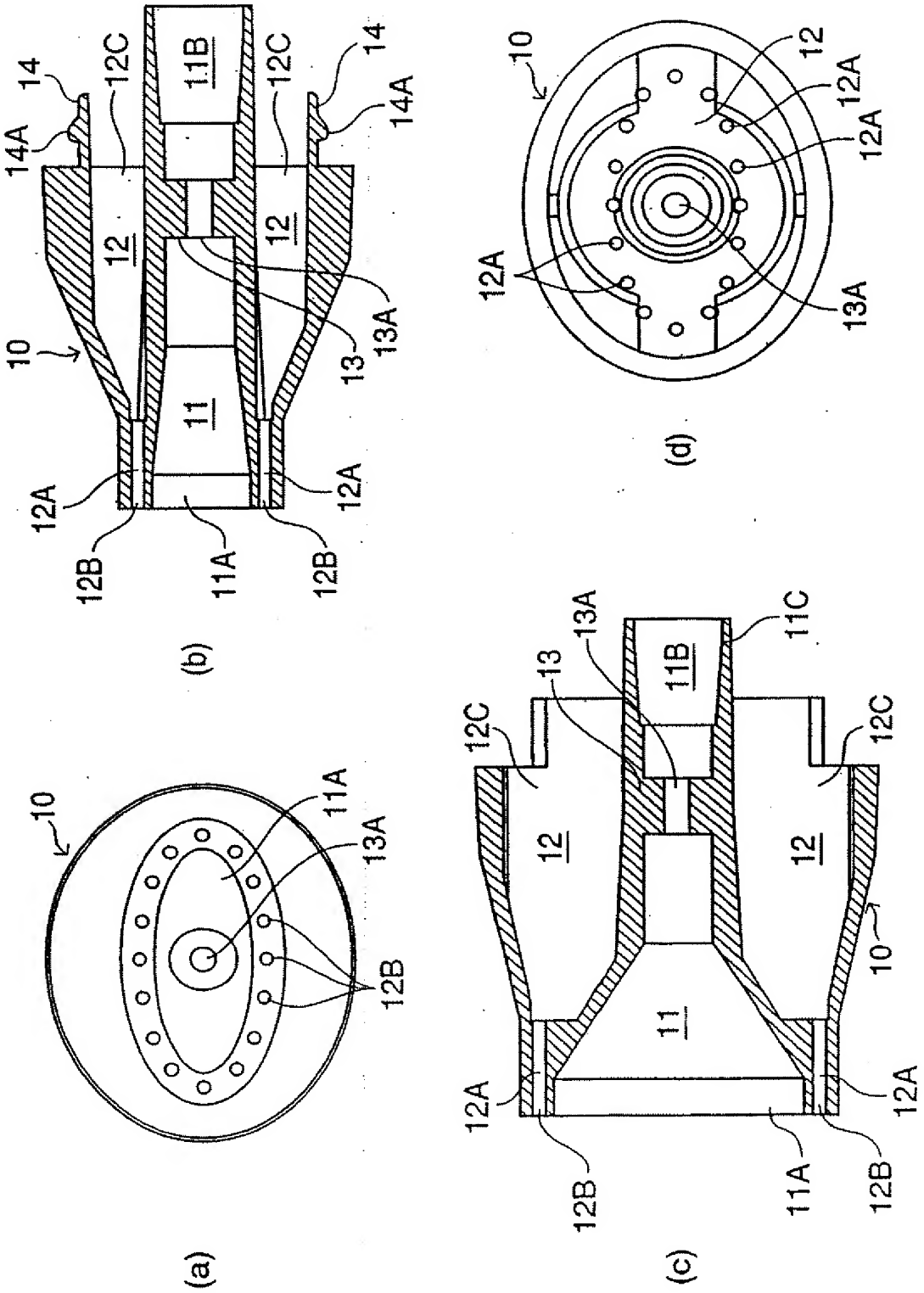
12A
12C

[Figure 4]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13
11
12A
12A
12B
11A
12B
(c)
13A
11C
13
11B
12C
12C
12
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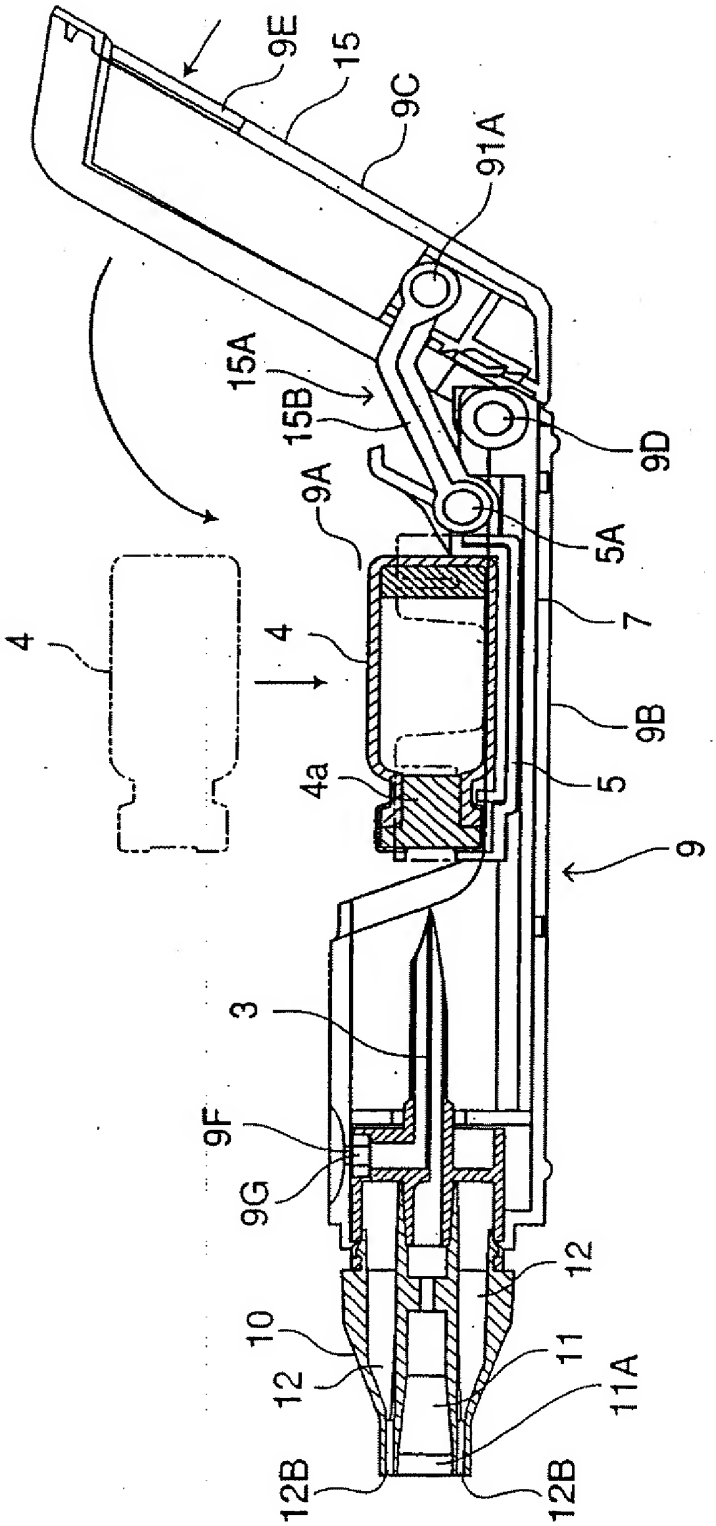
13A

[Figure 5]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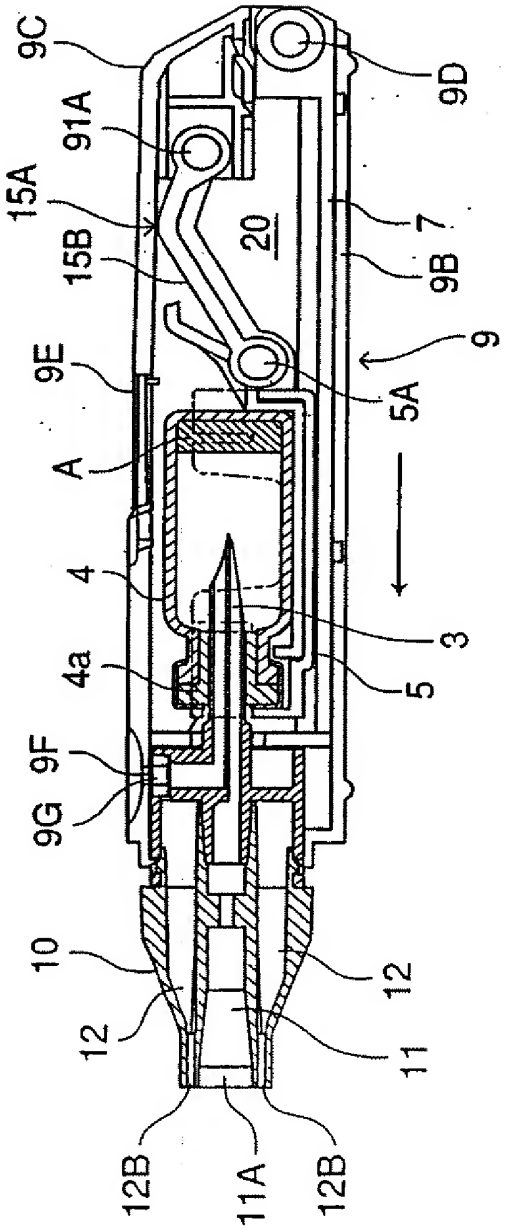
12B

[Figure 6]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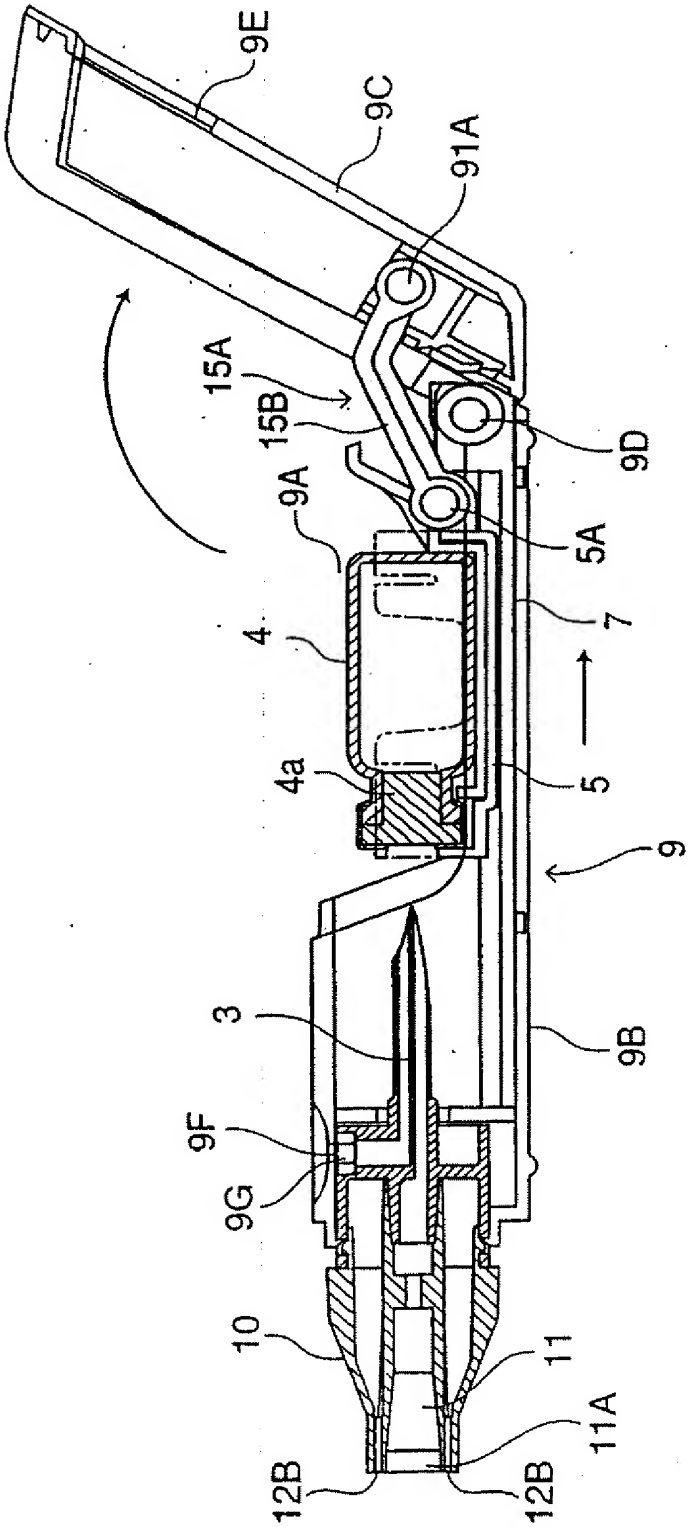
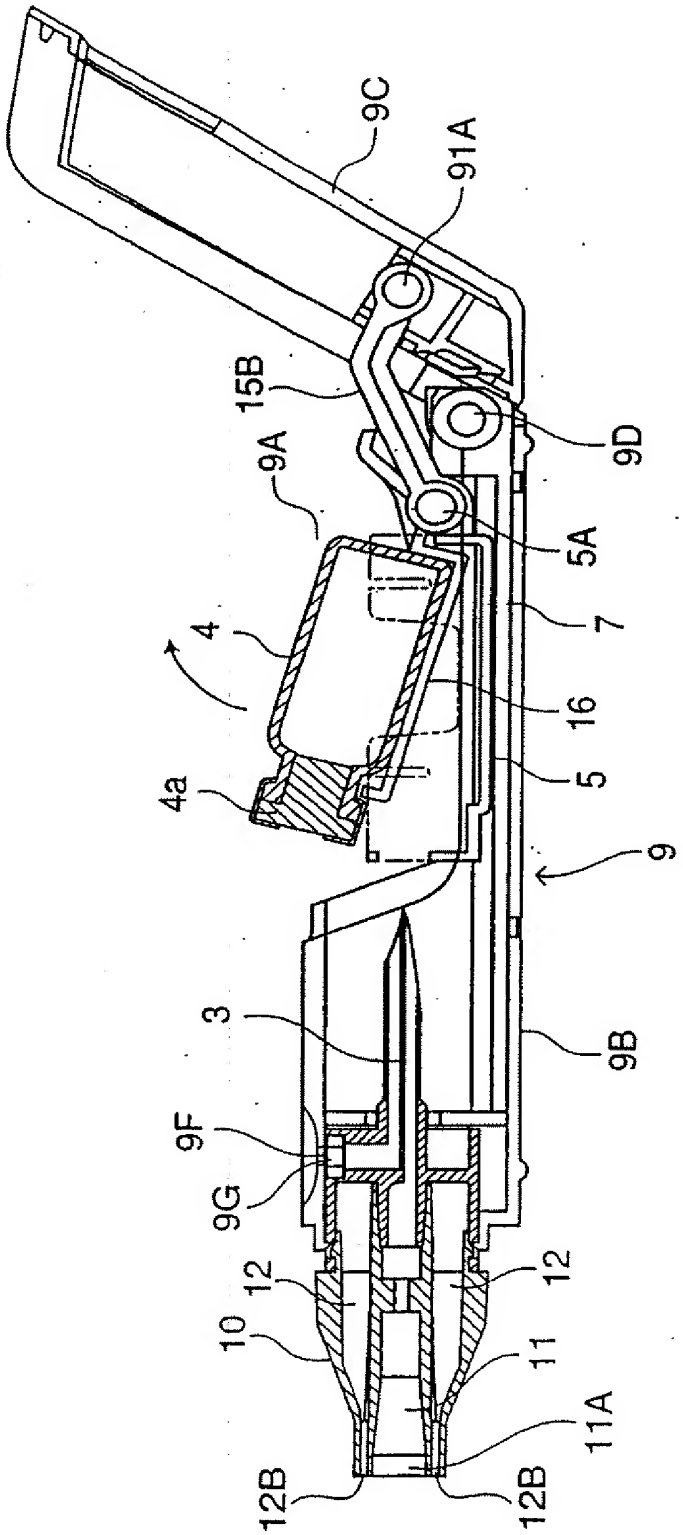
11A
12B

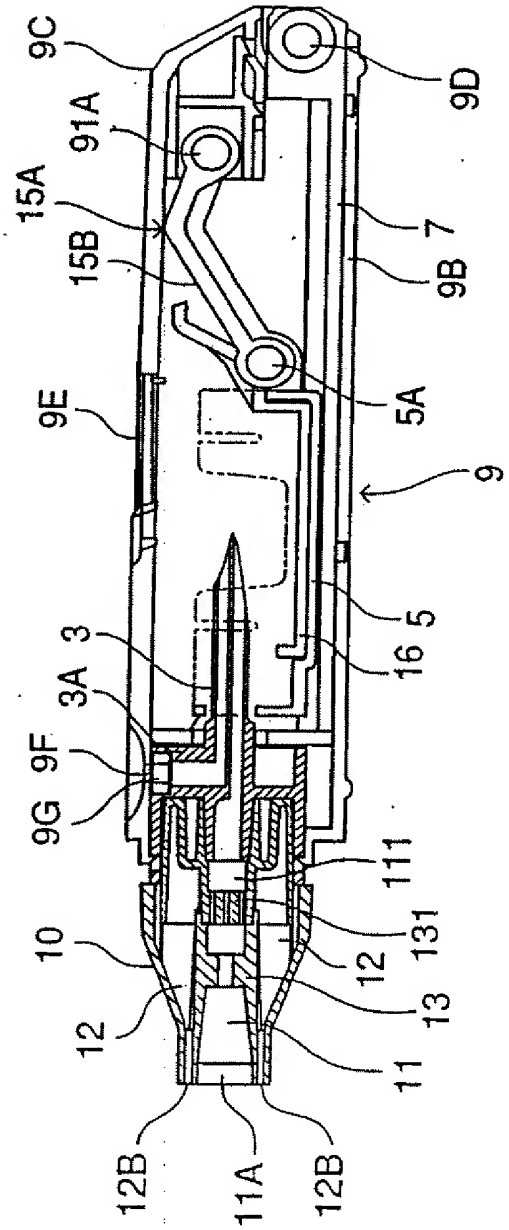
[Figure 7]



[Figure 8]



[Figure 9]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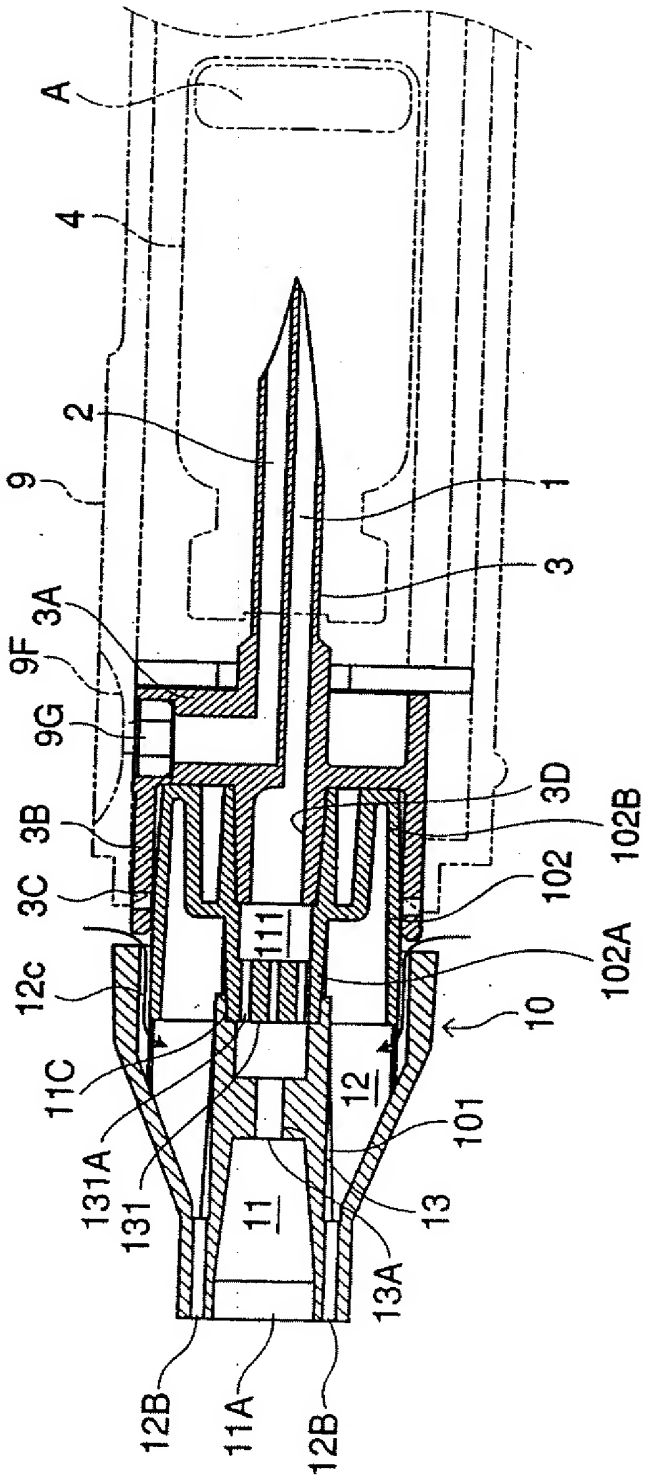
11A
12B

[Figure 10]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3B
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102A
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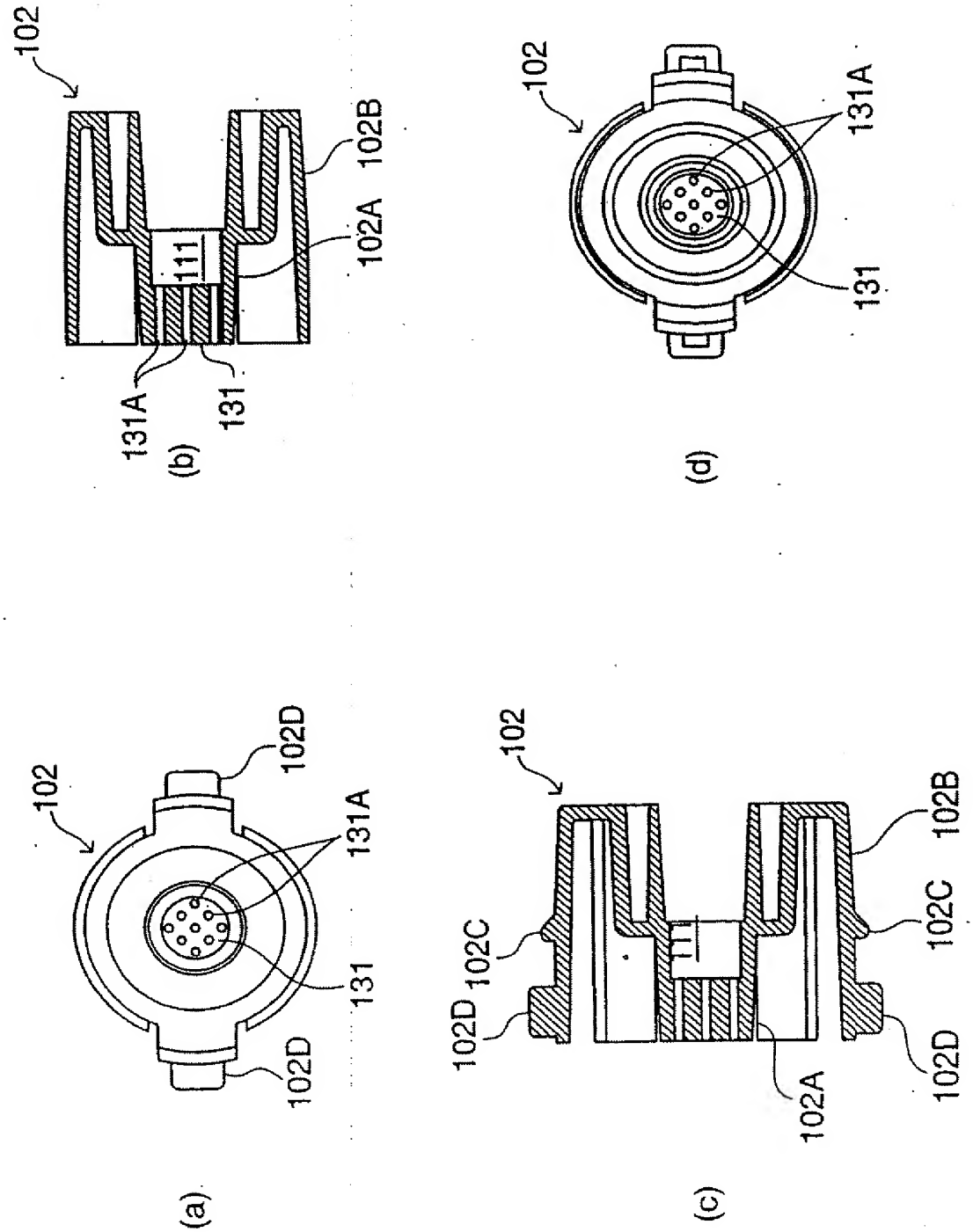
102B
3D
111

[Figure 11]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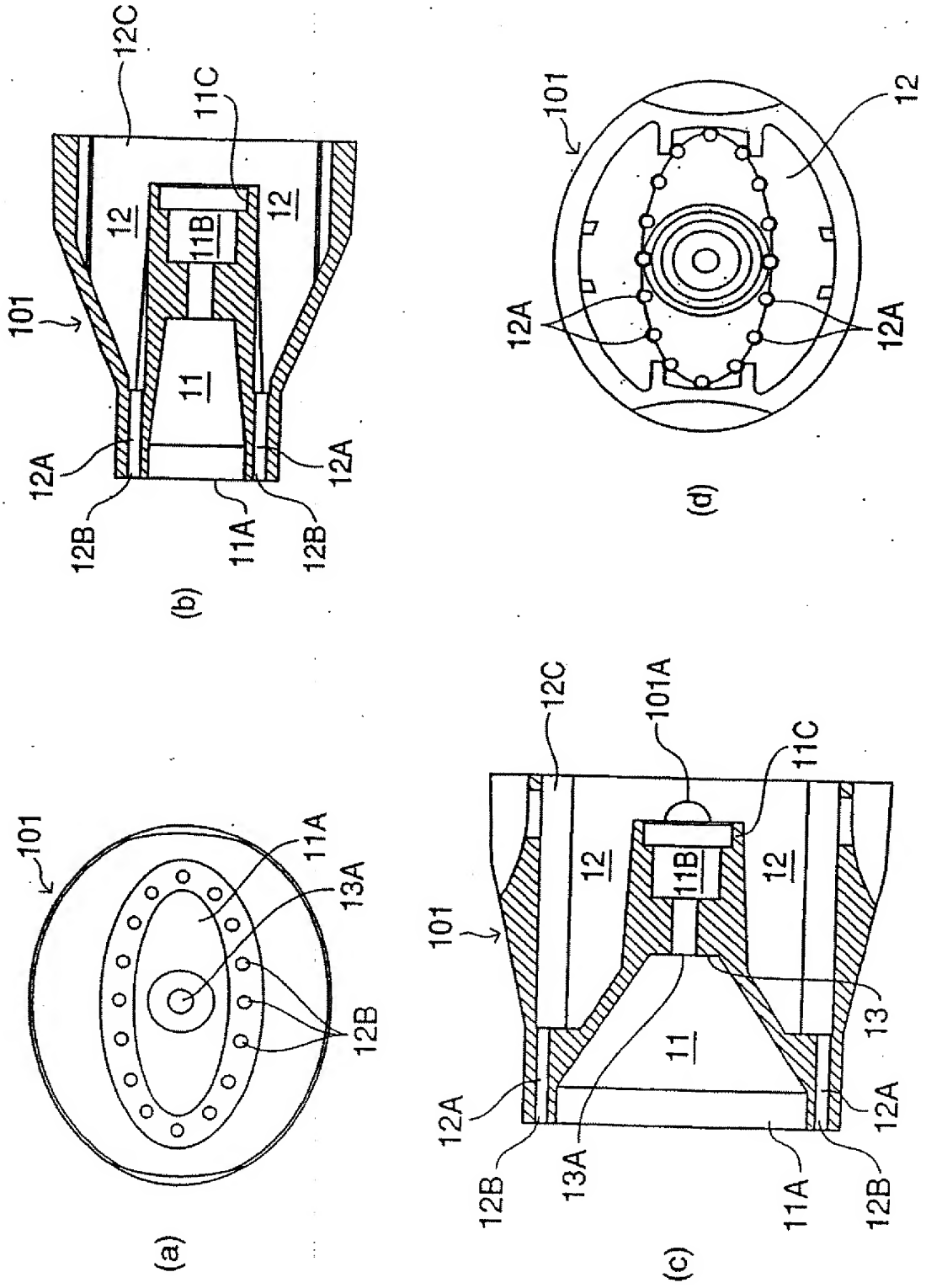
102
131A
131
(d)
102
102D
131A
131
102D
(a)
102
102B
102C
102C
102D
102D
102A
(c)

[Figure 12]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11B
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101
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12A
12A
12B
11A
12B
(b)
101
12
12A
12A
(d)
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11A
13A
12B
(a)
12C
101A
11C
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11B
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13A
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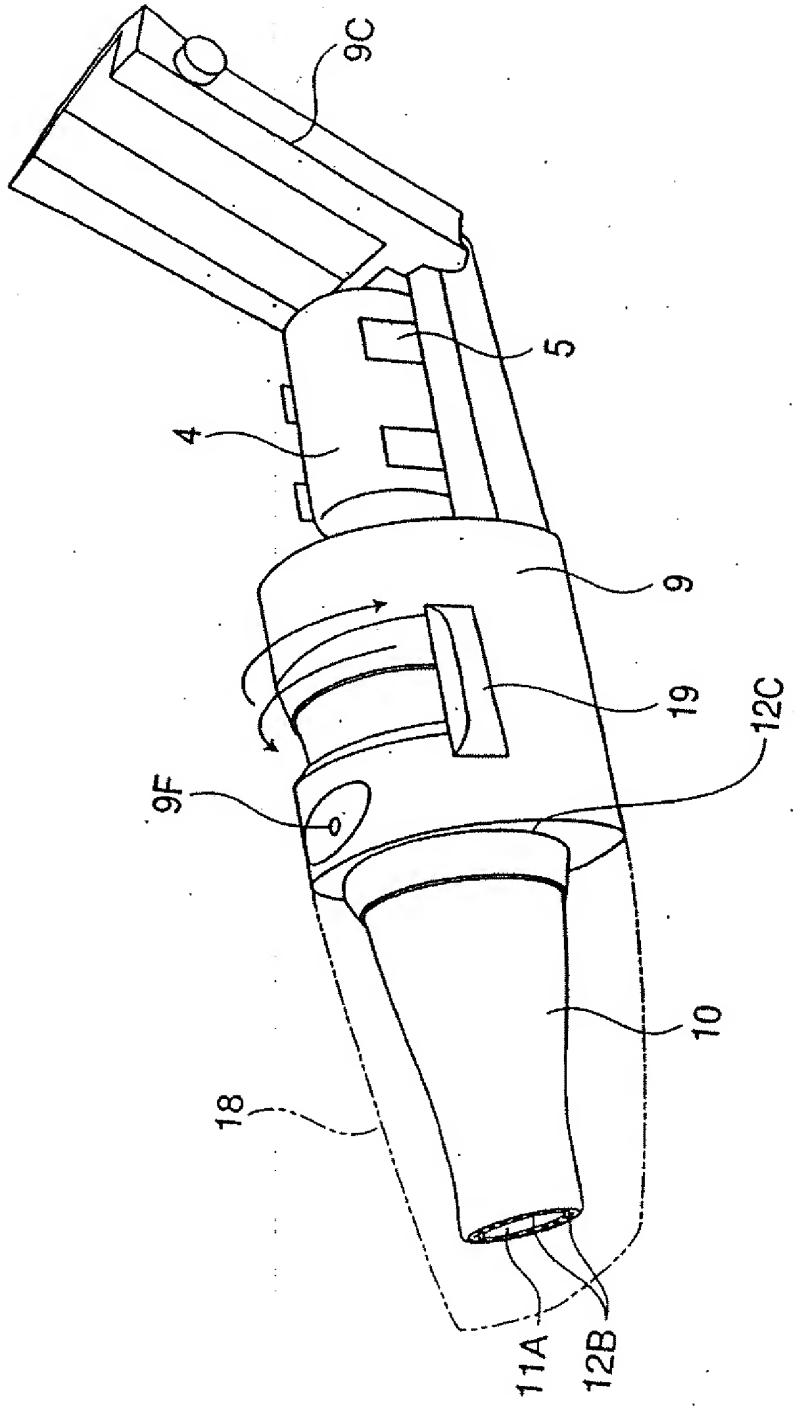
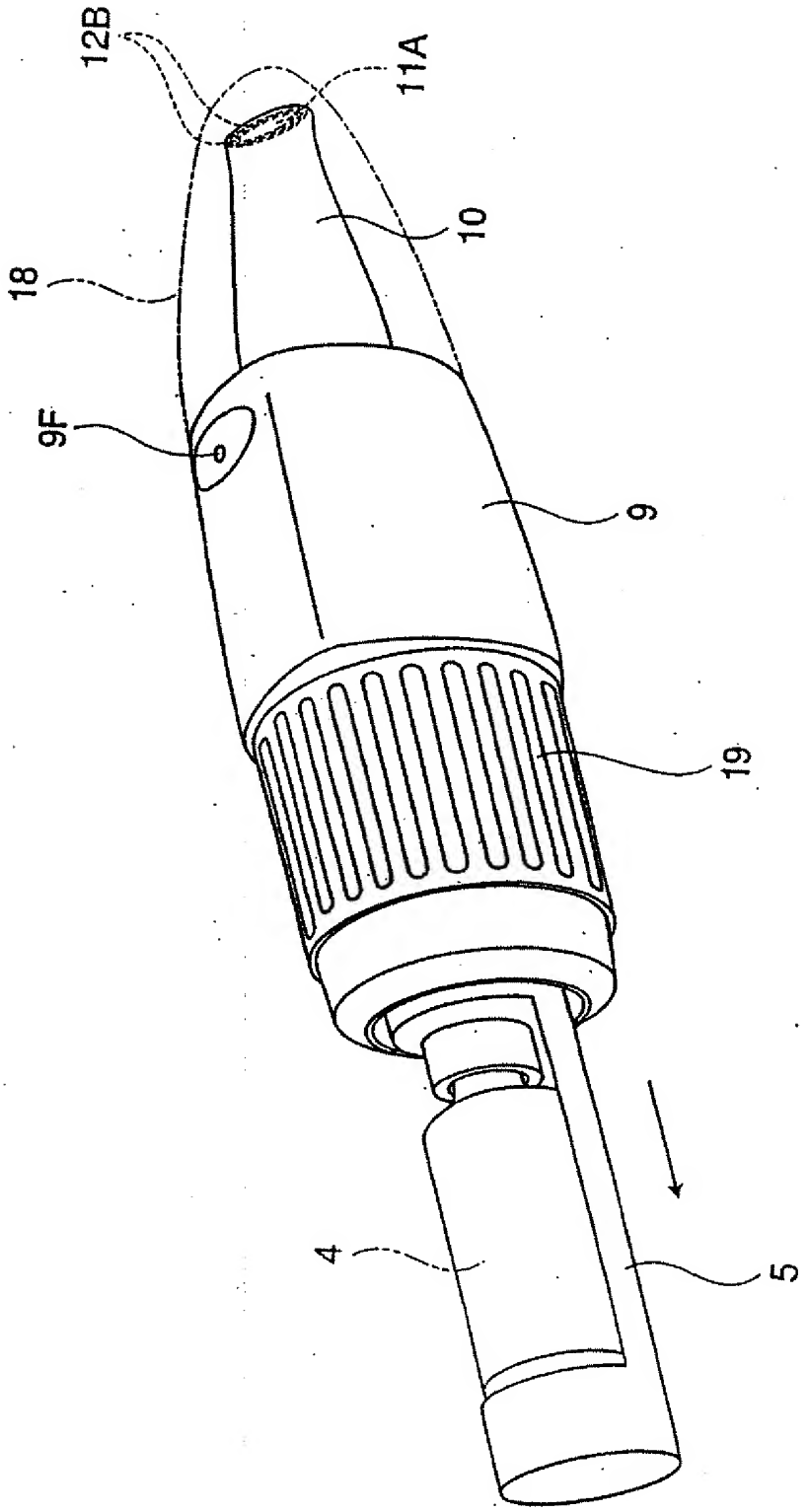
(c)

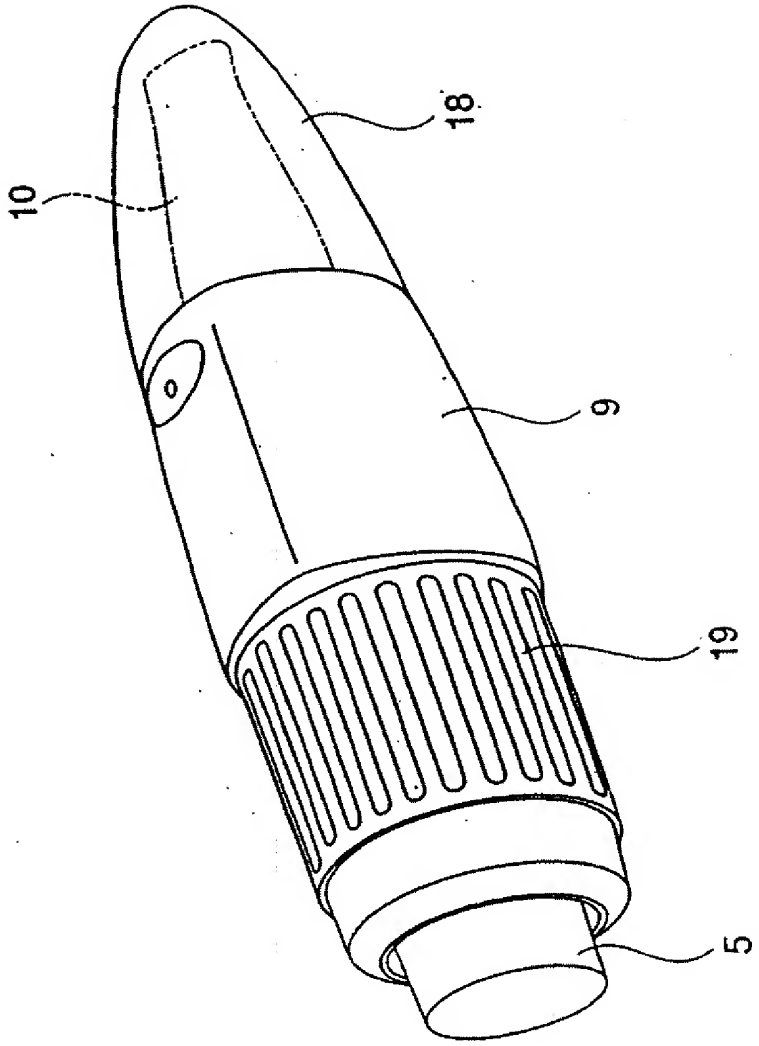
[Figure 13]



[Figure 14]



[Figure 15]



[Document Name] Abstract

[Summary]

[Object]

The present invention provides a inhalation device for transpulmonary administration which can prevent agglomerated masses of fine particles of the pharmaceutical composition from entering the user's (patient's) mouth.

[Method for Achieving the Object]

An inhalation device for transpulmonary administration comprising: a chamber for containing a pharmaceutical composition; an air inlet flow path for introducing to the chamber outside air to apply the air-generated impact to the pharmaceutical composition; an inhalation flow path for inhaling the pulverized pharmaceutical composition; a housing for accommodating the chamber, the air inlet flow path, and the inhalation flow path; a mouthpiece provided at one end of the housing, the mouthpiece being provided with a mouth-side flow path which communicates with the inhalation flow path and an auxiliary flow path for directly inhaling the outside air which does not communicate with the inhalation flow path and the mouth-side flow path. A mouthpiece of another aspect is provided with a mouth-side flow path which communicates with the inhalation flow path and a divider having an orifice in at least one of the mouth-side flow path or the inhalation flow path for reducing

the diameter of the flow path by forming a step part

[Selected Figure] Figure 3